NDA 18-140/S-027

Wyeth-Ayerst Research
Attention: Warren Sunshine
P.O. Box 42528
Philadelphia, PA 19101

Dear Mr. Sunshine:

Please refer to your supplemental new drug application dated August 27, 1998, received August 28, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ativan (lorazepam) Injection, 2 mg/mL and 4 mg/mL.

This supplemental new drug application provides revised annotated labeling that includes the addition of new text to the Geriatric Use subsection of the PRECAUTIONS section that conveys the safe and effective use of Ativan Injection in the geriatric population.

The specific statements that are added to the Geriatric subsection of labeling are described below:

1. "Clinical studies of Ativan generally were not adequate to determine whether subjects aged 65 and over respond differently than younger subjects; however, age . . . "

2. "Age does not appear to have a clinically significant effect on lorazepam kinetics (see "**CLINICAL PHARMACOLOGY**")."

3. "Clinical circumstances, some of which may be more common in the elderly, such as hepatic or renal impairment, should be considered. Greater sensitivity (e.g., sedation) of some older individuals cannot be ruled out. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range (see "**DOSAGE AND ADMINISTRATION**")."

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, this supplemental application is approved effective on the date of the letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (dated July 28, 1998).

Please submit the copy of final printed labeling (FPL) electronically to this application according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavyweight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 18-140/S-027." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Anna Marie Homonnay, Regulatory Health Project Manager, at (301) 594-2850.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Russell Katz

12/12/01 01:05:03 PM